Transplanted nonviable human hepatocytes produce appreciable serum albumin levels in mice.

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Public Summary:
The study reveals that transplantation of dead human hepatocytes into mice produces significant human albumin levels in their blood for at least 8 days. The finding cautions against using early time points to establish the therapeutic efficacy of hepatocytes derived from human pluripotent stem cells.

Scientific Abstract:
In animal models of liver cell therapy serum human albumin levels are universally measured as a marker for the engraftment and function of transplanted human hepatocytes, or hepatocyte-like cells derived from human stem cells. However, even the most efficient cell transplantation protocols encounter a significant amount of graft cell death. If albumin released from dying cells could be detected for prolonged periods of time in the serum of the recipient, it may misleadingly suggest engraftment and function of the transplanted cells. While a half-life of approximately 20 days of human albumin in humans is established, the duration of its detectability in mice is unknown. Here we show that human albumin is readily detectable in the serum of mice injected with nonviable human hepatocytes. Human albumin levels peak 24h after injection of hepatocyte debris, and remain detectable at significant levels for at least 8 days. Our finding suggests that long-term, or in situ, analyses are needed to prove functional engraftment of human primary or stem cell-derived hepatocytes.